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PATENT SPECIFICATION

NO DRAWINGS

Inventor: PHILIP SAXTON HARTLEY

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COMPLETE SPECIFICATION

Aerosols

We, BENGER LABORATORIES LIMITED, a British Company, of Holmes Chapel, Cheshire, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to substantially anhydrous pressurised aerosol powder formulations.

Pressurised aerosols are a form of packaging in which the material in liquid or finely divided form together with a liquefied gas or gas under pressure is contained in a can provided with a valve. The valve is generally a metering valve which delivers a specific dose. On opening the valve the pressure inside the can causes the contents to be discharged in the form of a fine spray or aerosol. The liquefied gas or gas under pressure is known as the propellant and is usually a fluorohydrocarbon or fluorohalohydrocarbon such as trichloromonofluoromethane, dichlorotetrafluoroethane and dichlorodifluoromethane.

The present invention is particularly concerned with solid finely divided pharmaceuticals suspended in an anhydrous medium containing the propellant, for use as an aerosol. Such aerosol formulations are particularly adapted for the treatment or relief of respiratory ailments, the aerosol being inhaled by the patient. The aerosol formulations may also be used in other ways, for example external application, where the pharmaceutical is appropriate for this purpose. The pharmaceuticals or medicaments are often polar in character, that is bear electro-positive and electro-negative charges on their surface, and are insoluble in the propellant, and in order to secure a satisfactory suspension of these materials in the propellant a suspending agent is necessary. For this purpose liquid non-ionic surface active agents have been used. The liquid non-ionic surface active agents require to be used in amount comprising at least about 0.1% by weight of the formulation, and generally are used in amount comprising 0.25—5% by weight of the formulation.

It will of course be readily appreciated that with any pharmaceutical preparation it is very desirable that the presence of chemicals other than the active ingredients, unless those chemicals are clearly merely inactive diluents, be reduced to the absolute minimum. It has now been found that the solid suspending agents comprising dialkyl sulphosuccinates and alkylbenzene sulphonates are exceptionally suitable for this purpose and can be used in amount comprising at least one-hundredth, and generally far less than this, of that required when using a liquid non-ionic surface active agent.

Accordingly the present invention is for a pressurised aerosol composition comprising a finely divided solid medicament having a particle size less than 100 microns, a substantially anhydrous propellant and a solid anionic surface active agent selected from the group comprising alkali metal, ammonium and amine salts of dialkyl sulphosuccinate, where the alkyl groups have 4—12 carbon atoms, and alkylbenzene sulphonic acid where the alkyl group has 8—14 carbon atoms. It is preferred to use the surface active agent in the form of the sodium salt, and this comprises desirably the sodium salt of dioctylsulphosuccinate, dibutylsulphosuccinate, dinonylsulphosuccinate, di-isobutylsulphosuccinate, dodecylbenzenesulphonic acid or decylbenzenesulphonic acid.

According to a preferred embodiment of the invention the solid anionic surface active agent is sodium dioctylsulphosuccinate.

[*Price*

The medicament is a finely divided solid, having a particle size of less than 100 microns, and preferably is of a particle size of 1—25 microns. Examples of medicaments which may be used include isoprenaline sulphate, atropine methonitrate, adrenaline acid tartrate, ephedrine hydrochloride, ergotamine tartrate, diphenhydramine hydrochloride, hydrocortisone acetate, antibiotics for example penicillins, streptomycin and tetracycline, and mixtures of any of these together or with other medicaments. The medicament suitably comprises 0.025—20% by weight of the total composition, although larger or smaller proportions may be used if desired. According to a preferred embodiment the total composition contains 0.1—2% of medicament.

The solid anionic surface active agent is used in very small amounts. The amount of the surface active agent required is related to the solids content of the suspension and to the particle size of the solids. In general it is only necessary to use 0.01—1% of the solid anionic surface active agent by weight of the solids content of the suspension; it is not necessary to use larger amounts than this and the use of amounts in excess of 5% of the solids content of the suspension is quite inappropriate. Thus for example with a suspension of a medicament for inhalation purposes where the composition contains 1% of solids of particle size about 10 microns, satisfactory suspension is obtained using 0.0005—0.002% of the solid anionic surface active agent by weight of the total composition.

The propellant may be any of the conventional propellants comprising for example fluorohydrocarbons or fluorohalohydrocarbons such as trichloromonofluoromethane, dichlorodifluoromethane, dichlorotetrafluoroethane, monochlorotrifluoromethane, monochlorodifluoromethane and mixtures of any of these together or with other propellants.

In some cases it may be desirable to add a polar solvent to the formulation; suitable polar solvents for this purpose include ethyl alcohol and isopropyl alcohol.

It may also be desired to add auxiliary solids to the formulation. Thus where the medicament is of density considerably less than that of the propellants, it may be suitable to add a solid inert diluent of high density of the same particle size, so that the density of the combined solids is similar to that of the propellants. Suitable inert solids for this purpose include sodium chloride and sodium sulphate.

The following examples are given to illustrate the present invention. The percentages are by weight.

EXAMPLE 1

The following composition was prepared and incorporated in a pressurised aerosol package.

	%
Isoprenaline sulphate (particle size 2—8 microns)	0.1
Atropine methonitrate (particle size 2—8 microns)	0.04
Sodium dioctylsulphosuccinate	0.002
Dichlorotetrafluoroethane	40
Dichlorodifluoromethane	to 100

This composition is useful for the relief of asthmatic conditions and used as an inhalant gives a dry spray which is readily absorbed by the mucous membranes.

EXAMPLE 2

	%
Isoprenaline sulphate (particle size 2—8 microns)	0.1
Atropine methonitrate (particle size 2—8 microns)	0.04
Sodium dibutylsulphosuccinate	0.002
Dichlorotetrafluoroethane	40.00
Dichlorodifluoromethane	to 100

This composition is useful for the relief of asthmatic conditions and used as an inhalant gives a dry spray which is readily absorbed by the mucous membranes.

EXAMPLE 3

	%
Ephedrine hydrochloride (particle size below 20 microns)	1.0
Sodium chloride (particle size below 20 microns)	1.0
Naphazoline nitrate (particle size below 20 microns)	0.1
Cineole	0.2
Sodium dioctylsulphosuccinate	0.015
Dichlorodifluoromethane	30.0
Dichlorotetrafluoroethane	to 100

This formulation is useful as a nasal decongestant.

EXAMPLE 4

	%
Ergotamine tartrate (particle size below 8 microns)	0.3
Sodium dioctylsulphosuccinate	0.003
Ethyl alcohol 74 O.P.	5.0
Dichlorotetrafluoroethane	35.0
Dichlorodifluoromethane	to 100

EXAMPLE 5

	%
Diphenhydramine hydrochloride (particle size below 25 microns)	0.5
Sodium dinonylsulphosuccinate	0.003
Ethyl alcohol 74 O.P.	2.5
Dichlorodifluoromethane	30.0
Dichlorotetrafluoroethane	to 100

EXAMPLE 6

	%
Hydrocortisone acetate (particle size below 25 microns)	0.4
Sodium dodecylbenzene sulphonate	0.004
Dichlorotetrafluoroethane	40.0
Dichlorodifluoromethane	to 100

WHAT WE CLAIM IS:—

1) A pressurised aerosol composition comprising a finely divided solid medicament having a particle size less than 100 microns, a substantially anhydrous propellant and a solid anionic surface active agent selected from the group comprising alkali metal, ammonium and amine salts of dialkyl sulphosuccinate, where the alkyl groups have 4—12 carbon atoms, and alkylbenzene sulphonic acid where the alkyl group has 8—14 carbon atoms.

2) A pressurised aerosol composition as claimed in claim 1 wherein the surface active agent is a salt of dioctylsulphosuccinate, dibutylsulphosuccinate, dinonylsulphosuccinate, di - isobutylsulphosuccinate, dodecylbenzenesulphonic acid or decylbenzenesulphonic acid.

3) A pressurised aerosol composition as claimed in claim 1 or claim 2 wherein the surface active agent is in the form of the sodium salt.

4) A pressurised aerosol composition as claimed in any of the preceding claims wherein the surface active agent is sodium dioctylsulphosuccinate.

5) A pressurised aerosol composition as claimed in any of the preceding claims wherein the medicament has a particle size of 1—25 microns.

6) A pressurised aerosol composition as claimed in any of the preceding claims wherein the medicament comprises 0.025—20% of the total composition.

7) A pressurised aerosol composition as claimed in claim 6 wherein the medicament comprises 0.1—2% of the total composition.

8) A pressurised aerosol composition as claimed in any of the preceding claims wherein the solid anionic surface active agent is used in amount comprising less than 5% by weight of the solids content of the composition.

9) A pressurised aerosol composition as claimed in claim 8 wherein the solid anionic surface active agent is used in amount comprising 0.01—1% by weight of the solids content of the composition.

10) A pressurised aerosol composition substantially as hereinbefore described.

11) A pressurised aerosol composition substantially as hereinbefore described and illustrated in any of the preceding examples.

F. MURPHY,
Agent for the Applicants,
Chartered Patent Agent,
Fisons Limited,
Harvest House,
Felixstowe, Suffolk.

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